Capacity and Inventory Optimization for Pharmaceutical Industry

by

Huong Thi Dang
Bachelor of Business Administration, National University of Singapore, 2013

and

Brett Anthony Elgersma
Bachelor of Science, Iowa State University, 2016

SUBMITTED TO THE PROGRAM IN SUPPLY CHAIN MANAGEMENT
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF APPLIED SCIENCE IN SUPPLY CHAIN MANAGEMENT
AT THE
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

May 2020

Signature of Author: _____
Department of Supply Chain Management
May 1, 2020

Signature of Author: _____
Department of Supply Chain Management
May 1, 2020

Certified by: _____
Dr. Nima Kazemi
Postdoctoral Associate, Center for Transportation and Logistics
Capstone Advisor

Accepted by: _____
Prof. Yossi Sheffi
Director, Center for Transportation and Logistics
Elisha Gray II Professor of Engineering Systems
Professor, Civil and Environmental Engineering

Capacity and Inventory Optimization for Pharmaceutical Industry

by

Huong Thi Dang

and

Brett Anthony Elgersma

Submitted to the Program in Supply Chain Management
on May 1, 2020 in Partial Fulfillment of the
Requirements for the Degree of Master of Applied Science in Supply Chain Management

ABSTRACT

The pharmaceutical industry is subject to many unique constraints, due in part to both product characteristics and regulatory guidelines. Nevertheless, pharmaceutical companies are expected to be able to serve customers that rely on their products, even as demand can be unpredictable and erratic. Pharmaceutical companies have choices in how they deal with demand uncertainty, but two schools of thought dominate: hold additional inventory or employ additional capacity. Finding the right balance between additional inventory and excess capacity proves difficult given product shelf-life constraints and long production ramp-up lead times. This study develops a mixed-integer linear program that optimizes inventory policy and production capacity policy under stochastic demand scenarios at a single node of the supply chain by minimizing inventory costs, production costs, and anticipated write-off costs. Scenarios of demand uncertainty with different probabilities are simulated to provide insights into key drivers of the model behavior and guide insights into useful inventory policies. Findings demonstrate that in an environment characterized by long production ramp-up lead times and products constrained by shelf life, neither additional inventory or excess production capacity alone is sufficient for hedging demand uncertainty. Therefore, pharmaceutical companies should consider employing the two strategies together to meet market demand with the optimal cost.

Capstone Advisor: Dr. Nima Kazemi
Title: Postdoctoral Associate, Center for Transportation and Logistics

ACKNOWLEDGMENTS

We would like to thank Dr. Nima Kazemi for guiding us through this process, challenging us to think differently, and pushing us to be the best versions of ourselves. Without his feedback and tutelage, we would still be trying to figure out where to begin. A special thank you is also due to Mr. Nicholas Wigdahl and the rest of the Supply Chain team at F. Hoffman-LaRoche Ltd. We appreciate your guidance through the intricate workings of pharmaceutical supply chains. Finally, we would like to thank our families, friends, and classmates for their patience, understanding, and support throughout this research process.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

1. INTRODUCTION

1.1 Motivation

On December 31, 2019, the Chinese government notified the World Health Organization (WHO) about a concentrated number of pneumonia cases it was tracking in the Hubei province. Just 71 days later, on March 11, 2020, the WHO declared a global pandemic based on the rapid spread of a novel coronavirus that was at the center of those first few pneumonia cases (*WHO Timeline—COVID-19*, n.d.). As the number of global cases grew, demand for medical supplies, including pharmaceuticals, skyrocketed. Along with focusing on developing vaccines and therapies for this new global health crisis, pharmaceutical companies also had to ensure the people they serve were able to maintain access to the products on which their well-being, and in some cases, their lives, depend. Is it possible for any industry to be prepared for such a major event?

The pharmaceutical industry has many unique facets that constrain its supply chain. One of the widely held missions of pharmaceutical companies is to develop medicines and other health products while ensuring that these products are accessible to patients, especially those products that are critical (*Operational Principles for Good Pharmaceutical Procurement*, n.d.). This principle makes it important that pharmaceutical companies can operate their supply chain to meet the urgent needs of patients, no matter what the circumstances. This challenge is made all the more difficult by the erratic demand fluctuations a product might experience in the early and later stages of the product life cycle. Most of the time, firms are unable to provide a highly accurate demand forecast when a product is first launched and they have little to no historical data. A similar problem arises when a product's patent expires and the market witnesses more competition from generic pharmaceutical manufacturers.

Another aspect that makes the pharmaceutical industry uniquely challenging is the regulatory burden that must be borne when manufacturing a pharmaceutical product. A strict production process must be certified and adhered to, lest the product fail to be deemed suitable for a destined market and have be discarded, resulting in significant financial losses. Failure of a company to have a product regulated leaves markets without access to much needed medications. If firms of fail to obtain regulatory approval, it causes uncertainty throughout the entire pharmaceutical industry, as competitor firms must step in to meet the demand for what are sometimes life-saving products.

Research and development are a major contributor to the cost of pharmaceutical products. They are also a source of great uncertainty. Because of the long lead times associated with pharmaceutical research and development cycles, a company may be very near having its production process certified when it decides that the commercial outlook for that product is not profitable. The decision of whether or not a firm will take a product to market is a great source of uncertainty that other firms in the industry need to safeguard against when making their strategic plans.

Finally, the limited shelf life of many drugs prevents pharmaceutical companies from stockpiling their products for fear that they might become obsolete. For many drugs, the clock starts ticking once the product is packaged, and each country regulates acceptable shelf lives in its own unique way. Product perishability, long Research & Development cycles, and extended production lead times create a challenge for industry players in designing a supply chain network to meet customer demand on time and in full without incurring extremely high production costs and an increased risk of write-off cost that comes with holding excessive amounts of safety stock.

These unique facets of the pharmaceutical industry create an environment that requires constant vigilance and the need for supply chain robustness in order to battle uncertainty. One way to buffer the uncertainties stemmed from customer demand, external supply, and internal production is to hold adequate levels of safety stock. Safety stock is also considered an effective tool in the case of the pharmaceutical industry to cover the long production lead time. The other way is to use excess production capacity as an alternative to inventory. By reserving excess production capacity, firms can reduce the high level of safety inventories and replace them with capacity utilization in times of high demand. Whether holding more stocks or reserving excess capacity, each approach has associated costs and specific impacts on the firm's strategy, which will be further discussed in the case of F.Hoffmann-La Roche Ltd. (Roche).

Roche, which was founded in 1896 with headquarters located in Basel, Switzerland , is a major player in the pharmaceutical industry and is well known for its remarkable customer service, a reputation that is achieved by having a very agile and responsive supply chain (*About Roche*, n.d.). The rest of this paper will be dedicated to ensuring Roche has the ability to maintain its pristine reputation in the most optimal fashion. Thorough literature will lay the groundwork for an appropriate model development, which will be analyzed and discussed in subsequent sections.

1.2 Problem Statement

Traditionally, Roche has tackled demand uncertainty by holding high levels of safety stock, which allows them to achieve an outstanding service level. Because of the high-profit margins that are characteristic of the pharmaceutical industry, it is understandable that Roche is willing to incur the necessary holding costs to ensure they always have enough stock to fulfill demand. However, Roche's current strategy is now being called into question, as there are competing interests among different stakeholders in the supply chain. Inventory managers are eager to reduce their inventory values in order to keep inventory investments as low as possible, while production managers seek to utilize capacity to the greatest extent possible in order to reduce unit costs.

1.3 Objective & Research Questions

This project addresses Roche's current supply chain dilemma: is it better to battle demand uncertainty by holding excess safety stock or by employing excess production capacity? Research will also address additional questions of interest. Specifically:

- Which parameters are sensitive to making this trade-off decision? Knowing how costs are affected will allow Roche to investigate the implementation of high-leverage, low-cost policies.
- Is accounting for demand uncertainty with only safety stock or only excess capacity an optimal solution?
- What is the best strategy to pursue in order to achieve supply chain optimization?

As demand uncertainty takes hold, especially when a product's patent expires in later product life cycle stages, the supply chain will need to be able to absorb demand uncertainty in order to maintain Roche's industry-wide reputation for service.

2. LITERATURE REVIEW

Supply chain optimization has long been a popular research theme; nevertheless, few works address the optimization problems in the pharmaceutical industry (Shah, 2004). Franco and Alfonso-Lizarazo (2017) categorize the recent quantitative works in pharmaceutical supply chain into three domains: supply chain network design, the inventory problem, and optimization of the supply network. Concerning the limited scope of Roche's problem, which primarily trades off between holding safety inventory and reserving excess capacity to guard against demand uncertainty, this review will discuss only the relevant works in supply chain operations that encompass inventory management, production planning, capacity expansion, and supply chain coordination.

To be able to recommend an optimal or near optimal strategy to prepare for demand uncertainty in a pharmaceutical supply chain it is important to understand the variables in play, the current consensus regarding inventory policy and aggregate production planning, and the efforts that have been undertaken to academically address this scenario thus far. First, we will look at definitions of concepts specific to the problem in question, such as inventory holding costs that are relevant to the pharmaceutical industry. Next, we will review work that studies the characteristics of inventory policies utilized by firms that produce products with a shelf life. We will recap common aggregate production planning methods, and focus on the method that is most practical for the scenario at hand. We will examine some of the impacts that the different aggregate production planning methods have with regard to the time they take to implement and what some of the constraints are. We will also look at some papers in capacity expansion and discuss their relevance to our project. Finally, we will review recent work pertaining to supply chain coordination in order to understand how decisions in each part of the supply chain are important determinants for the decisions to be made in other parts of the process.

2.1 Inventory Holding Costs

To understand the true trade-off between holding excess capacity or buffering uncertainty with a higher level of safety stock, it is important to ensure that the true costs of each are known and calculated appropriately. Silver, Pyke, and Thomas state that "the cost of carrying items in inventory includes the opportunity cost of the money invested, the expenses incurred in running a warehouse, handling and counting costs, the cost of special storage requirements, deterioration of the stock, damage, theft, obsolescence, insurance, and taxes (Silver, Pyke, & Thomas, 2017)." Roche experiences both warehousing and write-off costs, but neither of them is currently being accounted for. Depending on the product and the manufacturing stage that product is in, the product may need to be stored frozen, kept in cold storage or in a traditional dry warehouse setting. Our conversation with an expert in Roche revealed that CHF 50 million of excess and obsolete inventories was written off in 2018 (Source: Roche Cost-to-Serve Model). Therefore, it is important to consider both the cost of warehousing and the cost of potential write-off along with the cost of capital in order to truly understand the cost of holding inventory that Roche realizes.

Because of the shelf life constraint, and the potential of write-off that arises from this characteristic, it is important that any solution considers the best way to handle products with a shelf life. In the paper "Revisiting the shelf life constrained multi-product manufacturing problem," Sharma reviews the commonly adhered to methods for battling the probability of the shelf life expiring in a manufacturing setting. Specifically, the three methods mentioned are a reduction in cycle time, a reduction in production rate, or a simultaneous reduction in cycle time and production rate. Sharma contributes the fact that as

the production rate is decreased, the per unit cost rises. This rise in the per unit cost needs to be factored into the inventory holding cost once the decision is made to intentionally reduce the production rate (Sharma, 2009). Should Roche choose to combat product obsolescence by reducing the production rate, it is important to capture the increase in production cost so that the increased inventory holding cost can be appropriately accounted for.

2.2 Production Planning

An increase in inventory holding costs can cause severe damages on a company's financials, and the aggregate production strategy that a firm subscribes to plays a major role in determining inventory levels, and therefore inventory holding costs. Silver, Pyke, and Thomas (2017) describe two conventional strategies for aggregate production planning: level and chase. A level aggregate production strategy seeks to maintain a steady level of production throughout the year. Production continues in times of depressed demand that builds up inventories for times when demand outpaces production. This approach is typically utilized by firms that have a high barrier for onboarding additional employees, or firms that place a premium on retaining institutional knowledge. A chase aggregate production strategy seeks to minimize inventory levels by adapting the workforce size, and therefore capacity, to only produce what is demanded during the period in question. The strategy is common for industries that do not require extremely skilled labor, but experience very high holding costs.

A great example of a firm identifying and employing the appropriate production strategy is the Blue Bell case. In 1982 Blue Bell paid $21.9 million in net interest expenses compared to the $1.1 million they paid in net interest expenses in 1979 as a result of skyrocketing interest rates. This apparel company underwent a massive organizational change that focused on implementing a level production strategy, but also sought to minimize their overall inventory levels in order to minimize their inventory holding costs. The result of the project was a $115 million reduction in inventory in 21 months, which was a 31% reduction in less than two years (Edwards et al., 1985). This work is extremely relevant in showing that there is indeed a strong correlation between production capacity policy and inventory policy. Furthermore, it shows that adopting the proper strategy for both production capacity policy and inventory policy can lead to a minimal overall cost for the organization. Although it may not be immediately apparent, the pharmaceutical industry that Roche operates in shares key characteristics with the fashion industry. Rocephin, the product that is the main focus of this study, experiences very seasonal demand, the same way that certain clothing types might be more attractive during specific seasons. Additionally, because styles change frequently, excess apparel inventory degrades in value quite substantially after a sales season completes, which is similar to the shelf life constraint that pharmaceutical products experience. The Blue Bell case is a prime example of how a level production strategy can be successful in the type of environment Roche operates in. However, to be sure that a chase production strategy should be ruled out, another characteristic needs to be examined: Roche's ability or inability to quickly alter capacity.

2.3 Capacity Expansion

Because Roche will need to employ specialized labor if they wish to add additional mid-term capacity, and therefore endure a long lead time, it is necessary to review the research existing decision support models for capacity ramp-up. Although an existing repository of literature in production ramp-up has helped to resolve related problems of lot sizing, worker staffing, or production capacity decisions, the definition of production ramp-up in these papers is fundamentally different from the one in our research question. Glock & Grosse (2015) summarize the definition of production ramp-up across past papers as "the phase in the life cycle of a new product between the end of product development and full capacity production", which is not the case for our research product - Rocephin, as it is considered an established product of Roche. This leads us to the new literature strand of a capacity expansion problem. Capacity expansion is closely related topic to production ramp-up, but studies the decision of expanding capacity of a production system anytime there is a need to keep up with the increasing customer demand. A majority of academic work in the capacity expansion problem uses multi-factor models to aid the decision-making process (Julka et al., 2007). These models take different types of costs, demands, and socio-economic factors, such as employee skills, into consideration, and provide the output of how much capacity should be added in each manufacturing site. We will next review two papers that study the impact of inventory management and lead time in capacity expansion problem.

The first paper was written by Rajagopalan & Swaminathan in 2001. While most papers ignore the roles of inventory management in the capacity expansion problem, Rajagopalan & Swaminathan (2001) claim that inventory policies can have a considerable effect on any capacity expansion decision where demand grows gradually. Given the discrete characteristic of capacity additions, companies often face the problem of having excess capacity immediately after adding new capacity in production lines. Rajagopalan & Swaminathan (2001) argue that by producing in excess of demand and holding more safety stock, firms can delay the time of adding capacity; therefore, save the idle cost of excess capacity if they invest earlier. This paper is interesting as it studies the dynamic relationship between capacity and inventories, which is often ignored in capacity expansion models. However, the model does not include the importance of lead time in building up capacity, which, we believe, is crucial in our trade-off model for Roche.

The second paper written by Ryan (2004), on the other hand, emphasizes the need to meet a specified customer service level while calculating the risk of stockouts due to capacity shortage during capacity build-up lead time. She argues that capacity expansion decisions should be taken earlier, even when the firm still has excess capacity to meet current demand, because these current excess capacities will have to make up for the growth in demand during the lead time of additional capacity installations. While the paper is novel in introducing the lead time of installations into the capacity expansion problem, it does not study the interactions between capacity and inventories, as well as the role inventories can play to battle the uncertainty in demand over lead time. As stated previously Roche experiences high inventory holding costs given their cost of capital, cost of warehousing, and their potential write-off cost. They also experience some level of difficulty in scaling up production capacity in short and mid-term, so every effort should be undertaken to minimize the total costs resulted from both sides of the equation while maintaining the desired level of customer service. If the sole focus is on minimizing production cost and inventory holding cost, there is the possibility that Roche will find itself unprepared for demand anomalies it is ordinarily prepared to handle.

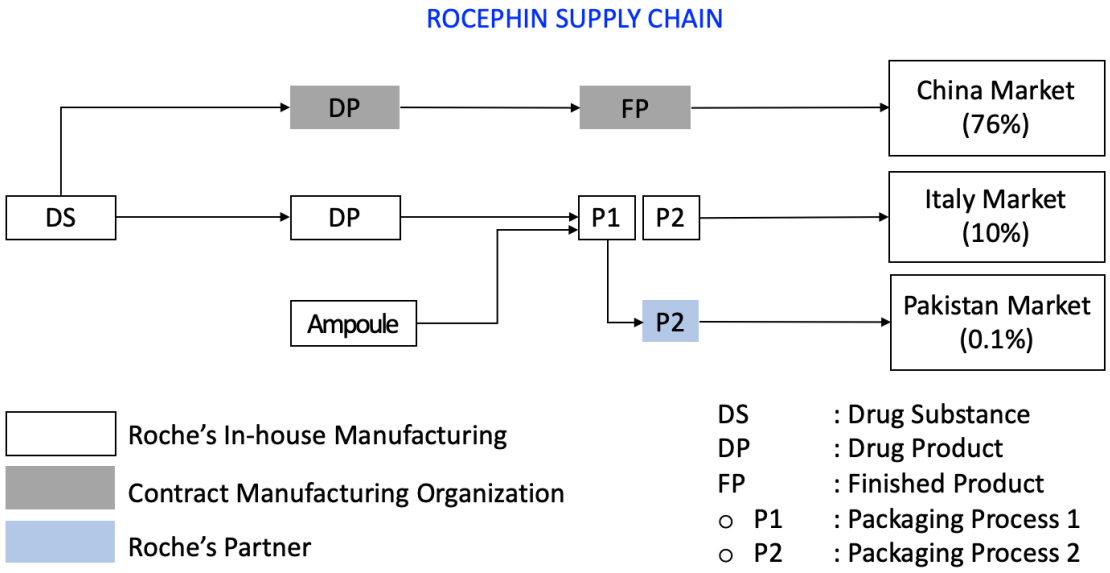
While there are works on pharmaceutical supply chain optimization, not many papers are directly related to our research problem. So far, we have reviewed the general literature work on inventory holding costs, production planning, and capacity expansion to have a better understanding of existing models that might provide insights into the challenges Roche currently faces. Going forward, by developing a mathematical model that minimzes the total cost of holding excess inventory and reserving flexible production capacity, we provide a new approach to the problem that many pharmaceutical companies are facing.

3. METHODOLOGY

This section details the process used to develop a mathematical model suited for answering the research questions outlined in Section 1.3. A description of a single product and its associated supply chain will be provided before examining methods of data collection. As the model is laid out, the various components will be discussed to provide a thorough understanding of how the model was developed. Finally, a hypothetical scenario will be set up to test the model's practicality and examine the model's sensitivity to each of the input parameters.

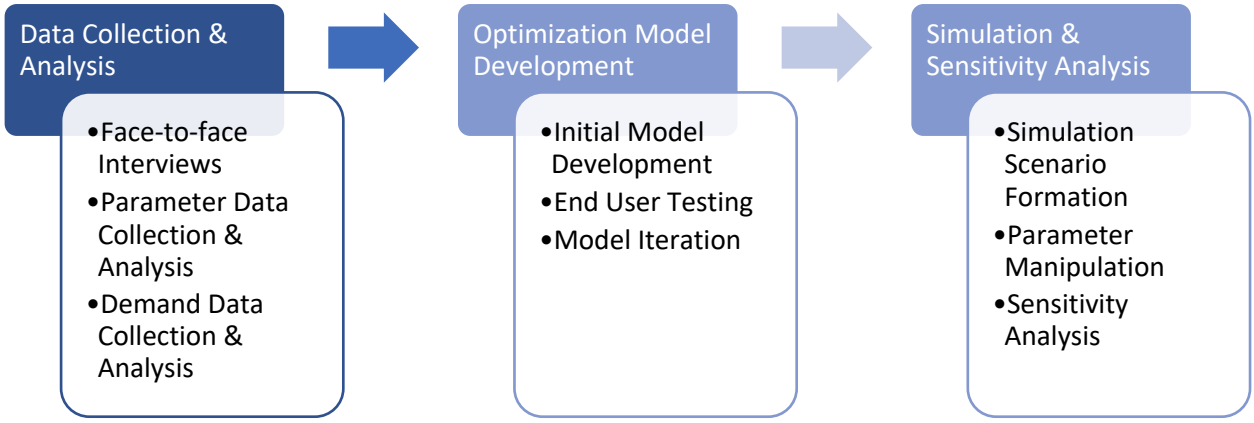
The project begins by examining one product, Rocephin, which is an antibiotic that is considered an established product in Roche's portfolio. Based on conversations with the Roche supply chain team, Rocephin was selected based on its relatively simple supply chain design. The simple supply chain allows for the creation and validation of a practical model that could be enhanced to allow for the additional complexities present in the supply chains of other products. The Rocephin sales markets that are initially in scope for this project are China, Italy, and Pakistan. These markets were chosen due to the importance of Rocephin in each of them. They are also unique with regard to the way Rocephin is delivered to the market in each country. The China market is a recipient of the active ingredient, known as the Drug Substance, but coordinates the container fill and packaging of the finished product. Filled containers are sold to Martin Dow, a separate entity that coordinates the final packaging and distribution to the Pakistan market. The Italian market receives completely packaged, finished product ready for distribution. As each market is served by a different supply chain, which is inherently composed of different players, production processes, and facility constraints, the trade-off question between inventory and capacity becomes unique. Examining the characteristics of each market help to ensure that the resulting model is not specifically tailored to anomalies that might be present in any one supply chain. Figure 1 outlines the Rocephin supply chain for each of the markets in focus.

Figure 1: Rocephin Supply Chain



An optimization model is the project's primary approach to resolving whether it is more appropriate to hedge demand uncertainty with inventory or with excess capacity. The model's inputs include deterministic parameters such as production throughput, product costs, inventory costs, etc., as well as stochastic demand information with known probabilities. The model's output is a set of decisions regarding inventories and capacity in order to minimize the total costs. Specifically, the model will provide: 1) a recommended shift matrix to employed throughout the scenario planning horizon, 2) a recommended inventory policy that compliments the recommended shift matrix, 3) and the total cost of the recommended plan. These outputs will provide strong analytical insights to decision-makers at Roche, and assist them in understanding the trade-off in the decisions they make every day. The project offers a new solution for a major problem that many pharmaceutical companies face, which is maintaining a high inventory level that comes with high inventory costs. By evaluating short-term inventory policy and mid-term capacity planning together, we provide a new decision-making tool to resolve the problem in a longer time horizon as compared to existing solutions. The steps taken to arrive at a final solution can be seen in Figure 2 and will be discussed at length in the subsequent sections.

Figure 2: Research Project Phases



3.1 Interviews and Data Collection

Creating a model for strategic decision making relies heavily on understanding the strategy of the company or industry for which the model is being created. To gain the most in-depth understanding possible, the team conducted onsite in-person interviews at Roche headquarters in Basel, Switzerland between October 14-16, 2019. A more profound understanding of how Roche's supply chain is composed, what the goals of the organization are, and what their strategy is to attain those goals was obtained by conducting interviews with the stakeholders noted in Table 1.

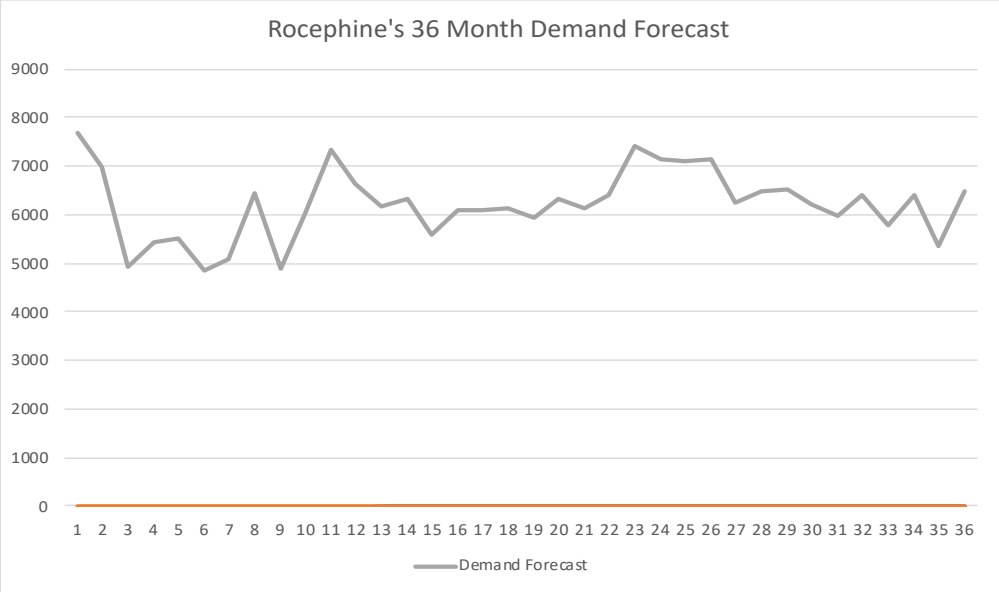
Table 1: Summary of Onsite Stakeholder Interviews at Roche from October 14-16, 2019

Role/ Interview Topic	**Interview Result**
Supply Planner	The process of translating unconstrained demand forecast from demand planners to replenishment plan to placing order
Demand Planner Europe	Understanding of Rocephin's demand trends and seasonality in top 3 big markets – China, Italy and Pakistan, and how demand forecast is derived
Supply Chain Finance	Rocephin's demand data, forecast accuracy, production and write-off costs
Network Planning	The financial and temporal trade-offs between inventory management and capacity planning at Roche
Product Supply Chain Owner	Rocephin's supply chain and product information
Cost-To-Serve Model	Different types of costs involved in Roche's supply chain such as logistics, packaging, and write-off costs
Inventory Reduction Program	Stakeholders and their views of Inventory Reduction Program
Business Process Analyst	Rocephin's manufacturing process at Roche's Kaiseraugst plant

The onsite interviews gave insight into what decisions can be made, what the parameters and variables of those decisions are, and what data exists to support the decision-making process. The following inputs are provided by Roche. The data was inspected and cleaned upon delivery, and was verified with Roche stakeholders. Since the data itself were clear and ready to be input into the model, no additional step was required for data cleaning or analyzing. The data obtained was immediately instrumental in testing the model that will be outlined in the next section.

1) **Base demand forecast for the next 36 months:**
   36 months of aggregated demand forecasts for all markets are given by Roche's demand planner. Figure 3 shows the monthly forecasted demand for Rocephin for three years. The demand is assumed to be seasonal, with the highest peaks in the early and end of each year, as is the case with Rocephin.

Figure 3: Rocephin's Demand Forecast for 36 Months



2) **Most updated Root Mean Square Errors of demand forecast from the last 36 months:**
Understanding the current demand forecast and the accuracy of that forecast – which is captured by forecast's Root Mean Squared Errors (RMSE) assists in constraining the model to have a certain level of safety stock to cover the variability in forecast accuracy.

3) **A set of scenarios within which the base demand forecast can be increased or decreased by a certain percentage and the probability of each scenario:**
A single base demand forecast does not provide the full picture of the future demand of the examined product as the market outlook may alter significantly due to the dynamic market competition. For instance, if a competitor's generic product passes the required quality test to replace Roche's product in some market channels, the demand forecast for the examined product will likely decrease. Therefore, Roche provided a set of demand scenarios with their probability on top of the base demand forecast to better capture the dynamics of the market.

4) **A set of shift patterns that Roche can operate and the production capacity and operation cost of each shift pattern:**
Shift patterns are characterized by the number of days worked during the week and the number of shifts that operate each day. Roche operates 8-hour shifts; therefore, a 5x2 shift pattern would result in 2 shifts per each of the 5 workdays per week. A set of available shift patterns is shown in Table 7 and 8 in the Appendix.

5) **Set-up cost and set-up lead time when Roche moves from one shift pattern to another:**
When demand changes, set-up cost and set-up lead time account for the additional financial and temporal costs of setting up new production capacity, especially when the new shift pattern has a higher throughput rate and requires additional labor. As noted in section 2.3 the pharmaceutical industry faces long production ramp-up lead times that force them into using a level production strategy rather than a chase production strategy.

6) **Item cost and inventory holding costs:**
   It is important to consider the ramifications that holding inventory would have on the total cost in order to make an effective trade-off. The cost of the product up to the current stage and the cost of holding inventory are provided to determine the financial burden that would be realized should the model converge on a solution that requires an increase in safety stock.

7) **Product shelf-life and the required remaining shelf-life it has to have to be sold in the market:**
   If an optimal solution does entail the use of safety stock, it is crucial to take the product shelf-life into account. Section 2.1 outlined the unique facet of the pharmaceutical industry and the fact that regulations require a certain proportion of the product's overall shelf-life to be available once the inventory is brought into a specific market. Each product has its own regulations and requirements, and the model allows users to adapt this parameter to different products and changing regulations.

8) **Beginning inventory position of the first period and its shelf-life:**
   The beginning inventory and its shelf-life are the first inputs to derive the probability of having to write inventory off and the associated write-off cost. If Roche has a high inventory position at the beginning and the optimal production capacity depicts a high production throughput, we expect the write-off probability will be high in the scenario where market demand is lower than the base forecast.

With the above data collected from Roche, we develop a mathematical optimization model that takes both production costs and inventory costs into consideration and determines the optimal production capacity that Roche should plan from month 1. The mathematical formulation of the model will be discussed in detail in Section 3.4.

3.2 Scope and Limitations

The model allows decision-makers to quickly trade-off between utilizing inventory or production capacity to cover demand uncertainty and achieve robustness within the supply chain. The model is, however, limited in scope to only assess one echelon of the pharmaceutical supply chain at a time. Specifically, we look at the Drug Substance echelon of Rocephin's supply chain in the example in Section 4. The model is also limited in that it does not address different types of inventory. While the model does take safety stock into account, there is not a clear distinction between safety stock, cycle stock, and anticipation stock. Also, because the model focuses on a single echelon, there is no accounting for pipeline stock within the model. Finally, the time horizon for the scope of the project is 36 months, corresponding to the 36-month forecast time horizon provided by Roche. This period length allows us to manipulate only the shift pattern, but not the number of production lines to change the total production capacity.

3.3 Assumptions

Some assumptions are made in order to build a simple trade-off model that is easy to understand and capture the essence of real life. The calculations and output from our model are contingent upon the following assumptions:

1) All input parameters are available to or obtainable by the end-user.

2) The examined product has fixed shelf-life, and if it is not delivered to the designated market with the required shelf-life remaining, the inventory will be discarded without any salvage value.
3) Demand is normally distributed with a standard deviation equal to the Root Mean Square Error (RMSE) provided by the end-user. Demand in each period is independent and identically distributed.
4) Production will follow a Level Production Strategy, as defined in Section 2.3, but if demand is less than scheduled production for the month and the produced units would be discarded, Roche would choose not to produce.
5) If a new shift pattern is selected and the total number of shifts per week is less than the incumbent shift pattern, there is no ramp-up time necessary and the new shift pattern can be enforced right away. This explains all the null values in Table 8: Shift Pattern Lead Time Matrix in the Appendix.
6) There is a non-linear relationship between total shifts and production output/ production cost; therefore, we cannot calculate production output/ production cost simply by multiplying the capacity and cost per shift with the total number of shifts in each shift pattern. For example, the cost of running production at weekends will be higher than on weekdays, or the worker wage for working night shifts will be higher than day shifts. Nevertheless, there will be no shift pattern that has a higher operating cost for lower production capacity or vice-versa. In other words, there is no dominating shift in the shift matrix.
7) The model end-user can assign the probability of a scenario occurring based on market research or other relevant data available to the end user. The model takes in one set of scenarios every time it runs. If there is additional information regarding market conditions as it gets nearer to the forecasted period, the user can input another set of scenarios again into the model.

3.4 Mathematical Formulation

To assist Roche in finding the most cost-effective way to ensure their supply chain is capable of handling scenarios of demand uncertainty, a mixed-integer linear program (MILP) was developed. MILP's are used when the variables of the model have either linear properties or integer properties (Pochet & Wolsey, 2006). The variables of the model will be discussed further in forthcoming sections, but for purposes of justification it is important to note that both integer and linear variables are present in Roche's capacity versus inventory decision. This section examines the constant parameters, the variables, the objective function of the model, and the constraints the model is subject to.

3.4.1 Notations

The MILP model uses 3 sets and indices, 20 parameters, a single decision variable, and 5 intermediate variables that are defined and described in Table 2, 3, 4, and 5, respectively. Table 5 shows a list of intermediate variables the model uses to arrive at the final decision variable.

Table 2: Notations for Sets and Indices

Sets	
I	Set of shift patterns
T	Set of periods (months)
S	Set of scenarios
Indices	
i	Shift patterns, $i \in I$
t	Time periods (months), $t \in T$
s	Scenarios, $s \in S$

Table 3: Notations for Parameters

Parameters	
D_t	Base forecasted demand in period t (units)
$RMSE$	Root Mean Squared Errors of demand forecast for last T periods
p_s	Probability of scenario s
i_s	Change of base demand forecast in scenario s (%)
C	Production capacity of current shift pattern per time period (units/period)
C_i	Production capacity of shift pattern i per time period (units/period)
sc_i	Fixed set-up cost of shift pattern i from current shift pattern ($)
δ_i	Lead time to set-up shift pattern i from current shift pattern ($)
oc_i	Operation cost of shift pattern i per time period ($/period)
oc	Operation cost of current shift pattern per time period ($/period)
c	Item cost ($/unit)
h	Annual inventory holding charge excluding write-off cost ($/$inventory/year)
a	Amount of inventory at the beginning of T periods (units)
asl	Average inventory shelf life at the beginning of T periods (periods) (Refer to the example calculation of $asl_{t,s}$ in Table 5)
msl	Maximum inventory shelf-life allowed for the product to be sold in market (periods) E.g. If the shelf-life of the examined product is 36 months, and the market authority requires there must be at least 70% of product shelf-life remained when it is sold: $msl = 36 \times (1 - 0.7) = 10.8$ (months) Therefore, when the inventory shelf-life is more than 10.8 months, it becomes obsolete.

Table 4: Notations for Decision Variables

Decision variables	
b_i	Binary variable indicating whether to choose shift pattern i

Table 5: Notations for Intermediate Calculations Variables

Intermediate variables	
$asl_{t,s}$	Average inventory shelf life at the beginning of period t in scenario s (periods) E.g. If there are 1000 units of inventory at the beginning of month 3 in scenario 4; 700 units were produced in month 2 and 300 units were produced in month 1: $asl_{3,4} = \frac{(700\times 0.5+300\times 1.5)}{1000} = 0.8$ (months) We assume that the shelf life of all the stocks produced in month t is 0.5 (months) at the beginning of month $t+1$
$rarsl_{t,s}$	Average remaining inventory shelf life at the end of period t in scenario s, rounded to the nearest integer (periods). Equation (5) elaborate in details how to calculate this variable.
$E[USold]_{ts}$	Expected units sold in the next $rarsl_{ts}$
end_{ts}	Ending inventory in period t in scenario s (units)
wo_{ts}	Inventory write-off in t + msl months in scenario s (units)

3.4.2 Objective Function

$$min \sum_{i \in I} sc_i b_i + \sum_{s \in S} p_s \left(\sum_{t \in T,\ t \le \delta_i} oc + \sum_{t \in T,\ t > \delta_i} oc_i \quad + \frac{1}{2}\, c \times h \left((1+i_s) \sum_{t \in T} D_t - \sum_{t \in T,\ t \le \delta_i} C - \sum_{t \in T, t > \delta_i} C_i \right) + c \sum_{t \in T} wo_{ts} \right) \quad (1)$$

The objective of the model (equation 1) is to minimize the total costs: the first term represents the cost of setting up optimal shift pattern, and the second term represents the production and holding inventory costs under all the stochastic demand scenarios. The model accounts for the production costs in two phases: during the ramp-up lead time when Roche still operates under the old normal shift pattern, and after the ramp-up lead time when the new shift pattern is in place. Inventory holding costs for all periods the model is calculated by multiplying the holding costs with the remaining inventory at the end of T periods, and adding in the inventory write-off cost that is computed separately for each time period. Except for the set-up cost that is deterministic based on the optimal shift pattern for all scenarios, all other mentioned costs are weighted by the probability of each scenario given by Roche.

Inventory write-off cost for each time period in each scenario is calculated by taking the number of units expected to be written off and multiply by the item cost up to the current production stage. The number of units expected to be written off is derived from equations (2) to (7).

$$wo_{t,s} = end_{t,s} - E[USold]_{t,s} \quad (2)$$

$$end_{t,s} = \begin{cases} a + \min(C, C_i) - (1+i_s) D_t & if\ t = 1 \\ E[USold]_{t-1,s} + \min(C, C_i) - (1+i_s) D_t & if\ 1 < t \le \delta_i \\ E[USold]_{t-1,s} + C_i - (1+i_s) D_t & if\ t > \delta_i \end{cases} \quad (3)$$

$$E[USold]_{t,s} = \sum_{t+1}^{t+1+rarsl_{t,s}} D_t - RMSE \times \sqrt{rarsl_{t,s}} \times G\left(\frac{end_{t,s} - \sum_{t+1}^{t+1+rarsl_{t,s}} D_t}{RMSE \times \sqrt{rarsl_{t,s}}}\right) \quad (4)$$

$$rarsl_{ts} = \left\lceil msl - max\left(0.5, \begin{cases} \frac{(0.5\times C)+(end_{ts}-C)\times(asl_{t-1,s}+1)}{end_{ts}} & if\ 1 \le t \le \delta_i \\ \frac{(0.5\times C)+(end_{ts}-C_i)\times(asl_{t-1,s}+1)}{end_{ts}} & if\ t > \delta_i \end{cases}\right)\right\rceil \quad (5)$$

$$D_t = D_{t-1} + \frac{\sum_{t\in T}(t-\bar{t})(D_t-\overline{D_t})}{\sum_{t\in T}(t-\bar{t})^2}\ if\ t > 36 \quad (6)$$

$$G(k) = NORMDIST\ (k, 0,1,0) - k * \left(1 - NORMSDIST(k)\right) \quad (7)$$

Subject to:

$$end_{ts} \ge 0 \qquad \forall t \in T;\ s \in S \quad (8)$$

$$b_i\ is\ binary \qquad \forall i \in I \quad (9)$$

$$\sum_{i\in I} b_i = 1 \quad (10)$$

Equation (2) determines the number of units expected to be written off in each period by subtracting the expected number of units to be sold from the number of units on hand at the end of that period.

The number of units on hand at the end of each period, in turn, is calculated slightly differently depending on the period the model is taking into consideration (3). For the first period, the units on hand will be the initial beginning inventory (a) plus any production that took place during that period $(\min(C, C_i))$ minus the demand for the first period $((1 + i_s)D_t)$. During the ramp-up or ramp-down lead time, the actual production is the lower value of the current production capacity and the new production capacity of the optimal shift pattern. This calculation aligns with the fifth assumption in Section 3.4. The assumption implies that there is no ramp-up time if the selected shift pattern has fewer number of shifts, and thus production capacity than the current shift pattern. It is important to note that the demand we use here has to adapt to each scenario by taking the forecasted demand multiplied by the change percentage for each scenario being calculated. Similar calculations are made for subsequent months with the only change being the beginning unit on hand is equal to the ending inventory from the previous period, which is equal to the expected unit sold from the previous period $(E[USold]_{t-1,s})$. Section B1 in Appendix B elaborates in detail how we arrive at this transformation.

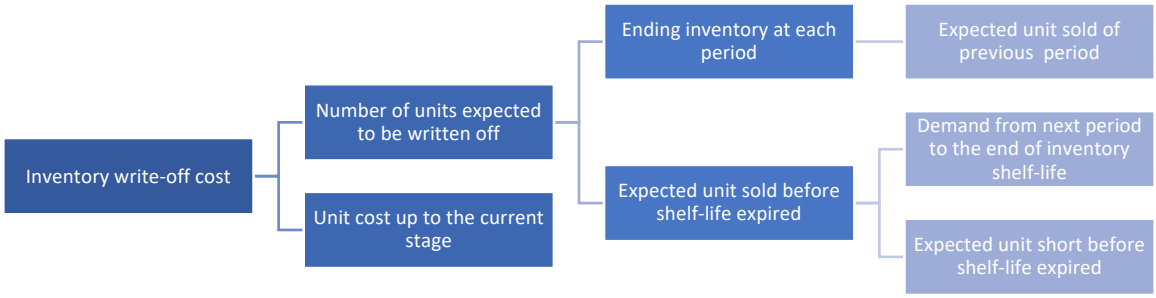
Equation (4) shows the steps to find the number of units sold for a given ending inventory in period t. First, the average remaining shelf-life of the inventory on hand at the end of each period is calculated and rounded to the nearest integer. After that, we compute the total demand for the period length during, which this ending inventory is not yet expired. The computation is done by summing all the periodic demands starting from the next period until the last period when the inventory reaches the end of its shelf-life. The number of expected units short is then subtracted from this aggregated demand by

applying the Unit Normal Loss Function (7) to the standard deviation of demand multiplied by the square root of the number of periods composing the average shelf-life remaining (Silver et al., 2017). We replace the demand standard deviation with demand Root Mean Square Error (RMSE), assuming that RMSE is representable of demand standard deviation when demand is normally distributed, and demand forecast is close to the mean of actual demand.

The calculation of the average remaining shelf-life of ending inventory for each period is shown in equation (5). If ending inventory is less than or equal to the produced inventory during the same period, the average inventory shelf-life is 0.5 periods (or months in this case). Otherwise, we average the shelf-life of newly produced inventory in the current period with the shelf-life old inventory in the previous period by their unit amount. The average shelf-life is then subtracted from the maximum shelf-life allowed in the market msl to derive the average remaining shelf-life of ending inventory. We round the result to the nearest integer so that it can be used for equation (4). Because the shelf-life remaining is likely extended beyond the 36-month horizon that the model considers, equation (6) assumes that the future demand profile based on the demand in the previous period and the slope of demand in T .

A step-by-step guide to calculate Inventory write-off cost is depicted in Figure 4.

Figure 4: Inventory Write-off Diagram



3.4.3 Constraints

The model is constrained to ensure that all outcomes are not only feasible but are also reflective of reality. Any feasible model output will need to ensure that all periodic demand is met under each of the probabilistic scenarios being considered (8). Final constraints impose binary constraints on shift pattern variables and ensure that one, and only one, shift is selected for each model output (9 and 10).

4. RESULTS, ANALYSIS, AND DISCUSSION

The model detailed in Section 3 allows the decision-maker to evaluate options for the most optimal shift matrix to implement, along with a complimentary inventory policy. The recommendation is tailored to a scenario set the decision-maker has complete control to specify, and recommends a solution based on the lowest total cost of production, inventory, and anticipated write-off costs. The model offers flexibility to consider multiple demand probabilities within one scenario and is also able to be run many times to evaluate different scenario sets. In this section, we will analyze the results of the model by examining one simple scenario that Roche often faces. We will also study the sensitivity of parameters Roche has control over, taking the time frame of the model into account.

4.1 Simulation Description

To illustrate how the model might be used for decision making at Roche, we consider a practical example of common industry conditions. For the basis of simulation, let us suppose that the pharmaceutical industry is composed of only two types of firms: innovators, who strive to create new patents and be the first to produce and supply to the market, and generic manufacturers, who are extremely efficient and produce pharmaceutical products at an extremely low cost. Innovators invest a large amount of capital into the invention of new products, and are rewarded for their innovation by being granted a patent that typically lasts 20 years (Research, 2020). At some point, the expiration of that patent comes into focus and the generic manufacturers eagerly await the date of expiration so they can manufacture the previously patented drug, sell it at a lower cost, and steal market share away from the innovation firm. Mirroring reality, and for the purposes of our simulation, Roche is known in the industry as an innovator. As an innovator, it often faces competition from generic manufacturers when their products reach the end of their patented life.

Based on the uncertainties outlined in Section 1.1, the simulation will consider Rocephin, and potential generic competition from 2 generic manufacturers under 2 different scenarios. At first, there is an estimated 50% chance that two generic manufacturing firms will enter the market and provide a generic replacement for the patented product. The current demand forecast takes this into account; therefore, there is neither an increase nor a decrease in the forecasted demand. The supply chain planners using the model have learned that there is a growing possibility that one of the generic manufacturers they believed would enter the market will encounter a delay in gaining regulatory approval. If they fail to enter the market, the demand forecast is estimated to be increased by 25%. Based on the knowledge the planners have at this point, they place a 40% probability on this scenario occurring. Finally, the planners recently had a meeting with senior leadership where everyone in the room was questioning whether or not the other competitor could really achieve the production costs necessary to be competitive in the market. Although they did not have any concrete data, they decided to incorporate the possibility that both competitors might fail to penetrate the market, which would result in a demand increase of 50%. Given that the probability of both competitors failing to enter the market is low, they assigned a probability of 10% to this scenario.

The model will then be updated and rerun for a second scenario, where the following week the supply chain planners learned that one of the generic manufacturers did, in fact, fail to gain regulatory approval. Because they have this updated information, they can go back and rerun the model with the

exact same parameters and an updated demand scenario profile. Because one of the generic manufacturers failed to obtain regulatory approval, there is no longer a 50% chance that their original demand forecast will come to fruition. Instead, they assign a 67% probability that demand will increase by 25% because of the failure of their competitor. There is still also a chance that the other generic manufacturer will decide not to enter the market, and they assign a 33% probability that this situation will occur.

4.2 Simulation Parameters

Using data generated by the researchers for testing purposes, the additional parameters needed to complete the model can be added to the demand scenario described in the previous section. These parameters can be found in Table 6.

Table 6: Simulation Scenario Parameters

Parameter Name	**Value**
Production Stage	Drug Substance
Current Shift Pattern	6x3
Demonstrated Hourly Throughput	1200
% Production Line Dedication	100%
Additional Cost per Shift	3000
Production Ramp-up Lead Time	3 Months
COGS to Current Stage	5
Product Life Cycle Segment	Resilient
Product Shelf Life	36
Required Shelf-Life When Delivered to Market	60%
Aggregate 3-year Demand	16,200,000
Forecast Error	100,000
Cost of Capital	8.50%
Logistics and Warehousing as % of COGS	1.50%
Customer Service Level Target	98%

4.3 Simulation Results

The model laid out in Section 3 was adapted into a user-friendly Excel workbook to accommodate the preferences of Roche decision-makers. The workbook was created to act as a decision support tool that gives immediate feedback and utilizes the Solver add-on to converge on optimal solutions. The demand scenarios from Section 4.1 and the parameters from Section 4.2 were entered into the decision support tool. The model was then run, and the output was analyzed.

The original scenario appears to be primarily dominated by the 50% probability that there will not be any substantial increase in demand. Because Rocephin is in its “Resilient”, or end of life, stage and demand is waning, the model recommends a reduction in the number of weekly shifts from 18 to 12, but to buffer the potential for increased demand by holding additional inventory. Table 7 defines this additional inventory as “Anticipation Stock”, and also details the recommended shift pattern to be

implemented immediately, the percentage of the inventory that is anticipated to be written off, the immediate investment in additional capacity and inventory, and the total cost to the supply chain throughout the planning horizon.

Table 7: Original Scenario Simulation Results

Anticipation Stock	658,800
Shift Pattern	6x2
Write-off Probability	0.324%
Required Initial Investment	329,400.00 CHF
Total Supply Chain Cost	5,880,674.75 CHF

The scenario that was updated to reflect the loss of a competitor yields a different outcome. In the updated scenario, the model is no longer dominated by the probability that nothing will happen. The known demand increase forces the model to recommend 14 shifts per week, or a 7x2 shift matrix. Because there will be more production capacity throughout the planning horizon than in the original scenario, the need for Anticipation Stock is reduced below the level of the original scenario. This reduction in Anticipation stock also yields a reduction in anticipated write-offs and a lower upfront cost, although the total cost to the supply chain throughout the planning horizon will be higher. Table 8, below, defines the output from the model for the updated scenario.

Table 8: Updated Scenario Simulation Results

Anticipation Stock	620,100
Shift Pattern	7x2
Write-off Probability	0.00%
Required Initial Investment	310,050.00 CHF
Total Supply Chain Cost	6,326,050.00 CHF

4.4 Model Parameter Sensitivity

While the model will provide an optimal recommendation, given the input parameters selected, the output may not be acceptable for the Roche planners. Given the 36-month planning horizon the model is considering, there are only 3 parameters Roche is able to alter in order to achieve a more favorable outcome: the percentage of line dedication, the forecast error, and the customer service level target. The other input parameters are either determined by the product being planned or attempting to alter them would take considerable coordination and capital investment that would stretch beyond the planning horizon. In this section, the sensitivity of the 3 parameters Roche can change is tested and analyzed.

For the purposes of this sensitivity analysis, the parameters that are not being analyzed will be the same parameters used for the original simulation in Section 4.3, and can be found in Table 9 . These parameters will be fixed and will remain the same, while the 3 parameters being tested will be altered in various combinations. Table 10 shows the combinations of parameters being tested and analyzed, with

the first column indicating the parameter being tested and the remaining columns indicating the values that will be used while testing the indicated parameter.

Table 9: Constant Parameters for Sensitivity Analysis

Parameter Name	**Value**
Production Stage	Drug Substance
Current Shift Pattern	6x3
Demonstrated Hourly Throughput	1200
Additional Cost per Shift	3000
Production Ramp-up Lead Time	3 Months
COGS to Current Stage	5
Product Life Cycle Segment	Resilient
Product Shelf Life	36
Required Shelf-Life When Delivered to Market	60%
Aggregate Demand	16,200,000
Cost of Capital	8.50%
Logistics and Warehousing	1.50%

Table 10: Variable Parameters for Sensitivity Analysis

Parameter	**% Production Line Dedication**	**Forecast Error (RMSE)**	**Customer Service Level Target**
% Production Line Dedication	100%/ 75%/ 50%	100,000	98%
Forecast Error (RMSE)	100%	100,000/ 90,000/ 80,000	98%
Customer Service Level Target	100%	100,000	99%/ 98%/ 95%

4.4.1 Production Line Dedication

Using the constant parameters from Table 9 above, the decision support tool described in Section 4.3 was run 3 times, using 100%, 75%, and 50% Production Line Dedication. The resulting inventory policy, recommended shift pattern, and associated supply chain costs can be found in Table 11.

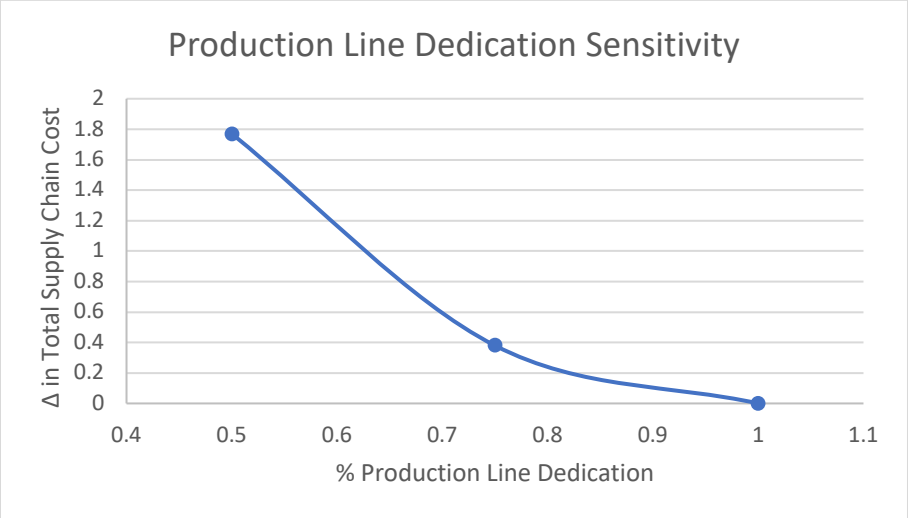
Table 11: % Production Line Dedication Sensitivity Results

% Line Production Line Dedication	100%	75%	50%
Anticipation Stock	658,800	1,782,000	4,215,600
Shift Pattern	6x2	5x3	7x3
Write-off Probability	0.324%	0.631%	3.818%
Required Initial Investment	329,400.00 CHF	891,000.00 CHF	3,394,800.00 CHF
Total Supply Chain Cost (TSCC)	5,880,674.75 CHF	8,098,256.24 CHF	16,302,387.11 CHF
% Change of TSCC	0%	38%	177%

Not surprisingly, as the % Production Line Dedication decreases, the number of shifts required to meet demand increases. As the data shows, at some point the maximum number of shifts is reached and, given the limited production line dedication to the production being planned, the only way to buffer the uncertainty of demand is by holding an increased amount of Anticipation Stock.

Figure 5 shows the relationship between the percentage of the production line dedicated to the product being planned for and the change in the total supply chain cost, which is the sum of production costs, inventory costs, and write-off costs. As Figure 5 shows, the relationship between the two variables is non-linear, meaning that an increase of 1% Production Line Dedication results in an exponential decrease in total supply chain costs.

Figure 5: Relationship Between % Production Line Dedication and Total Supply Chain Costs



4.4.2 Forecast Error

The same process of using the decision support tool was used to test changes in Forecast Error. The model outputs for the Forecast Error testing can be found in Table 12.

Table 12: Forecast Error Sensitivity Results

Forecast Error (RMSE)	100,000	90,000	75,000
Anticipation Stock	658,800	658,800	658,800
Shift Pattern	6x2	6x2	6x2
Write-off Probability	0.324%	0.319%	0.313%
Required Initial Investment	329,400.00 CHF	329,040.00 CHF	329,040.00 CHF
Total Supply Chain Cost (TSCC)	5,880,674.75 CHF	5,875,259.69 CHF	5,867,445.79 CHF
% Change of TSCC	0%	-0.09%	-0.22%

Sensitivity testing of the Forecast Error yielded an interesting result. Surprisingly, the model is not sensitive to the Forecast Error. Whether the Forecast Error was improved by 10% or 25%, the recommended shift pattern and inventory policy remained the same. The improved Forecast Error slightly improved the amount of inventory that would be anticipated to be written off, which subsequently reduced the total expected supply chain cost, but the improvements were marginal compared to the improvements that would need to be made to the forecast accuracy.

4.4.3 Customer Service Level Target

The sensitivity testing process was repeated a third time, this time testing changes in the Customer Service Level Target. The model outputs for the Customer Service Level Target testing can be observed in Table 13.

Table 13: Customer Service Level Target Sensitivity Results

Customer Service Level Target	98%	99%	95%
Anticipation Stock	658,800	658,800	658,800
Shift Pattern	6x2	6x2	6x2
Write-off Probability	0.324%	0.324%	0.324%
Required Initial Investment	329,400.00 CHF	329,400.00 CHF	329,400.00 CHF
Total Supply Chain Cost (TSCC)	5,880,674.75 CHF	5,880,674.75 CHF	5,880,674.75 CHF
% Change of TSCC	0%	0%	0%

Similar to the results for the Forecast Error testing, the model appears to be insensitive to changes in the Customer Service Level Target. This can be explained by observing that the model is not constrained by holding a minimum level of Anticipation Stock. Rather, the optimal outcome for the prescribed scenario utilizes a mix of Anticipation Stock and excess production capacity to account for demand uncertainty. Were the model constrained by requiring a minimum amount of Anticipation Stock to be held to account for the production ramp-up lead time, incremental changes to the Customer Service Level Target would be reflected in incremental changes to the required Anticipation Stock to be held.

4.5 Insights and Management Recommendations

Studying the sensitivity of the Production Line Dedication Percentage, the Forecast Error, and the Customer Service Level has been instrumental in being able to offer Roche decision-makers guidance. Supply chain practitioners often place great importance on improving forecast accuracy. Still, as the sensitivity analysis has shown, monthly forecast accuracy is not overly critical when considering strategic decisions regarding capacity and inventory policy. The same can be said with regard to Customer Service Level. This is not to say that the appropriate Customer Service Level and a highly accurate forecast are not crucial having an extremely efficient supply chain. Rather, they are important at the operational levels of the firm.

At the strategic level, where decisions between trading off capacity for inventory are made, the parameters that impact an optimal solution the most are, themselves, strategic. The simulation conducted in Sections 4.1 through 4.3 shows that accurate market intelligence is more beneficial than a precise demand forecast when it comes to strategic planning. The sensitivity analysis shows that having the right production mix and allocating production lines are a key driver in reducing your total costs while bracing for demand uncertainties. Understanding the aspects that are of importance in battling demand uncertainty will allow decision-makers at Roche to focus their time and investments on projects and policies that have the highest impact.

5. CONCLUSION

In this project, we developed a MILP optimization model that provides an optimal trade-off between holding additional safety stocks or employing excess capacity under stochastic demand conditions. The model outcome does not recommend combating demand uncertainty by solely adding additional capacity or only holding additional inventory. Rather, the optimal outcome is some combination of both inventory and excess capacity, which is constrained by the production ramp-up lead time and the shelf-life of the product.

While the model is useful for examining a single node in the supply chain, the model is limited in accounting for factors both upstream and downstream from the node being examined. A recommended path for future research would be to pursue concepts related to supply chain coordination. The given model could be further developed to derive an optimal solution with regard to inventory policy and production capacity policy taking inputs from each node of the supply chain into account. Furthermore, future models may be able to incorporate different supply chain designs into account, including dual-source supply chains, which would allow planners and managers to make further strategic use of the model.

This work serves to fill a gap in supply chain research with respect to trade-off decisions between utilizing inventory or capacity under uncertain demand conditions, specifically in the pharmaceutical industry. While the research is focused on one product for one pharmaceutical company, the model presented here is generalizable to the pharmaceutical industry as a whole, as well as other industries that might face similar product shelf lives, such as the apparel industry.

As future research into strategic trade-off decisions in the pharmaceutical industry is certain to continue in the future, this model will serve as a launching point from which to start. The simple step-by-step decision support model that was developed in conjunction with this paper will allow decision-makers at Roche to quickly arrive at a strategic direction that will ensure their customers' demands are being met with the service they have become accustomed to at an optimal cost.

REFERENCES

About Roche. (n.d.). Retrieved April 29, 2020, from https://www.roche.com/about.htm

Edwards, J. R., Wagner, H. M., & Wood, W. P. (1985). Blue Bell Trims Its Inventory. *Interfaces*, *15*(1), 34–52. https://doi.org/10.1287/inte.15.1.34

Franco, C., & Alfonso-Lizarazo, E. (2017). A structured review of quantitative models of the pharmaceutical supply chain. *Complexity*, *2017*. Scopus. https://doi.org/10.1155/2017/5297406

Glock, C. H., & Grosse, E. H. (2015). Decision support models for production ramp-up: A systematic literature review. *International Journal of Production Research*, *53*(21), 6637–6651. https://doi.org/10.1080/00207543.2015.1064185

Julka, N., Baines, T., Tjahjono, B., Lendermann, P., & Vitanov, V. (2007). A review of multi-factor capacity expansion models for manufacturing plants: Searching for a holistic decision aid. *International Journal of Production Economics*, *106*(2), 607–621. https://doi.org/10.1016/j.ijpe.2006.08.002

Operational Principles for Good Pharmaceutical Procurement. (n.d.). Retrieved December 4, 2019, from https://apps.who.int/medicinedocs/en/d/Jwhozip49e/

Pochet, Y., & Wolsey, L. A. (Eds.). (2006). Mixed Integer Programming Algorithms. In *Production Planning by Mixed Integer Programming* (pp. 77–113). Springer. https://doi.org/10.1007/0-387-33477-7_4

Rajagopalan, S., & Swaminathan, J. M. (2001). A Coordinated Production Planning Model with Capacity Expansion and Inventory Management. *Management Science*, *47*(11), 1562–1580. https://doi.org/10.1287/mnsc.47.11.1562.10254

Research, C. for D. E. and. (2020). Frequently Asked Questions on Patents and Exclusivity. *FDA*. https://www.fda.gov/drugs/development-approval-process-drugs/frequently-asked-questions-patents-and-exclusivity

Ryan, S. M. (2004). Capacity Expansion for Random Exponential Demand Growth with Lead Times. *Management Science*, *50*(6), 740–748. https://doi.org/10.1287/mnsc.1030.0187

Shah, N. (2004). Pharmaceutical supply chains: Key issues and strategies for optimisation. *Computers & Chemical Engineering*, *28*(6), 929–941. https://doi.org/10.1016/j.compchemeng.2003.09.022

Sharma, S. (2009). Revisiting the shelf life constrained multi-product manufacturing problem. *European Journal of Operational Research*, *193*(1), 129–139. https://doi.org/10.1016/j.ejor.2007.10.045

Silver, E. A., Pyke, D. F., & Thomas, D. J. (Writer on business logistics). (2017). *Inventory and production management in supply chains* (Dewey Library - Reserve Stacks HD40.S55 2017). Boca Raton : CRC Press, Taylor & Francis Group, [2017].

WHO Timeline—COVID-19. (n.d.). Retrieved April 10, 2020, from https://www.who.int/news-room/detail/08-04-2020-who-timeline---covid-19

APPENDIX A

Table 14 shows an example of 3-year monthly demand forecast data given by Roche in the beginning of Year 1. An example of other decision constants provided by Roche are illustrated in Table 15. Tables 16 and 17 denote examples of lead time changes and fixed cost changes, respectively, when shifting from one shift pattern to another.

Table 14: Example of Roche's 36-period Product/Market Forecast

Year	Month	Demand Forecast	Year	Month	Demand Forecast	Year	Month	Demand Forecast
1	Jan	7695	2	Jan	6153	3	Jan	7083
1	Feb	7003	2	Feb	6336	3	Feb	7158
1	Mar	4909	2	Mar	5605	3	Mar	6253
1	Apr	5435	2	Apr	6091	3	Apr	6478
1	May	5492	2	May	6082	3	May	6537
1	Jun	4843	2	Jun	6132	3	Jun	6211
1	Jul	5099	2	Jul	5928	3	Jul	5983
1	Aug	6442	2	Aug	6336	3	Aug	6413
1	Sep	4894	2	Sep	6134	3	Sep	5787
1	Oct	6006	2	Oct	6410	3	Oct	6405
1	Nov	7336	2	Nov	7403	3	Nov	5359
1	Dec	6644	2	Dec	7125	3	Dec	6498
	Total	**71799.00**		Total	**75734.00**		Total	**76166.00**

Table 15: Example of Roche's Other Decision Constants

Constant Variables	Value
Current Shift Pattern	2 shifts x 5 workdays
Monthly Production Throughput	1000 units
Monthly Production Costs	2000 CHF
Inventory Cost to Current Stage	5 CHF
Product Shelf-life	24 months
Required Shelf-life Remaining	60%
Cost of Capital	8.50%
Cost of Warehousing and Logistics	1.50%
Customer Service Level	98%

Market Scenario	Demand Change	Probability
1	-10%	50%
2	25%	40%
3	50%	10%
4	0%	0%
5	0%	0%
	Total	**100%**

Table 16: Shift Pattern Production Throughput and Cost Matrix

Shift Pattern	Monthly Production Throughput (units)	Monthly Production Costs (CHF)
5x2	40000	100000
5x3	58000	150000
6x2	48000	120000
6x3	70000	180000
7x2	56000	140000
7x3	80000	210000

Table 17: Shift Pattern Lead Time Matrix

Shift Pattern Change Leadtime (months)						
Future Shift Pattern / Current Shift Pattern	5x2	5x3	6x2	6x3	7x2	7x3
5x2	0	1	2	3	4	6
5x3	0	0	0	2	4	6
6x2	0	0	0	2	3	3
6x3	0	0	0	0	0	2
7x2	0	2	0	1	0	2
7x3	0	0	0	0	0	0

Table 9: Shift Pattern Fixed Cost Matrix

Shift Pattern Change Fixed Costs (CHF)						
Future Shift Pattern / Current Shift Pattern	5x2	5x3	6x2	6x3	7x2	7x3
5x2	0	10000	25000	35000	40000	45000
5x3	5000	0	35000	30000	40000	45000
6x2	5000	10000	0	10000	20000	30000
6x3	7000	10000	5000	0	10000	10000
7x2	10000	12000	5000	7000	0	10000
7x3	15000	10000	7000	5000	5000	0

APPENDIX B

B1. Beginning Inventory Calculation

$$Beginning\ Inventory_{t,s} = \begin{cases} a & if\ t = 1 \\ E[USold]_{t-1,s} & if\ t > 1 \end{cases} \quad (11)$$

1) $t = 1$:
   Beginning inventory $(t) = a$
2) $t > 1$:
   Beginning inventory (t) = Ending inventory $(t-1)$ – Expected unit long $(t-1)$ (*)
   = Ending inventory $(t-1)$ – (Ending inventory $(t-1)$ – Expected unit sold $(t-1)$)
   = Expected unit sold $(t-1)$)

Equation (11) elaborates how we calculate the inventory at the beginning of period t in any scenario s. If it is the first period, the beginning inventory is given by a. Otherwise, the beginning inventory is the ending inventory in previous period (t-1) subtracted from the expected unit long of period (t-1). Expected unit long $(t-1)$ is subtracted from Ending inventory $(t-1)$ to avoid double counting of the inventory amount that is going to be written-off as its shelf-life exceed the maximum allowed shelf-life msl. By expanding expected unit long (t-1), we simplify the whole calculation to expected unit sold of period (t-1).